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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,716	01/28/2002	Kenji Asano	0230-0160P	3342

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EXAMINER

YAO, LEI

ART UNIT PAPER NUMBER

1642

DATE MAILED: 12/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/856,716	<b>Applicant(s)</b> ASANO ET AL.	
	<b>Examiner</b> Lei Yao, Ph.D.	<b>Art Unit</b> 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 05 October 2005.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-4 is/are pending in the application.
- 4a) Of the above claim(s) 3 and 4 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-2 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>7/26/04, 5/25/01</u> . | 6) <input checked="" type="checkbox"/> Other: <u>exhibit A</u> .                        |

***DETAILED ACTION***

Amendment filed on 10/5/05 in response to the previous Non-Final Office Action (4/6/05) is acknowledged and has been entered.

Claims 1 and 2 have been amended. Claims 3-4 have been withdrawn for non-elected invention. Claims 1-4 are pending and claims 3-4 are withdrawn for non-elected invention and claims 1-2 are under consideration.

**The text of those sections of Title 35, U.S.Code not included in this action can be found in the prior Office Action.**

The following office action contains NEW GROUNDS of rejection.

**Rejections Withdrawn**

1. The rejection of claim 1 under 35 USC § 102 (b) as being anticipated by Mule et al., (Current Protocol in Immunology, unit 7.7, page 7.7.1-7.7.5 and unit 7.18, page 7.18.1-7.18-7, 1991) is withdrawn in view of the amendments to the claim.
2. The rejection of claims 1-2 under 35 USC § 103 as being unpatentable over Mule et al., (Current Protocol in Immunology, unit 7.7, page 7.7.1-7.7.5 and unit 7.18, page 7.18.1-7.18-7, 1991) and further in view of Yamamoto et al., (Biosci Biotechno Biochem, vol 61, p1909-1912, 1997) is withdrawn in view of the amendments to the claims.

**The Following is a New Ground of rejection**

1. ***As drawn to new matter***

***Claim Rejections - 35 USC § 112***

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It is noted that the claim 2 as newly amended claim recites **"raising the temperature of said suspension to 80-100°C to ensure inactivation of the enzymes"**, which is not supported by instant specification. Instant specification as filed, although provide a method as **"heated to a temperature of 95°C to ensure inactivation of the enzymes"** at page 9 as filed, does not provide sufficient support for the instant claims reciting **"raising the temperature of said suspension to 80-100°C to ensure inactivation of the enzymes"** in claim 2.

## **2. Rejection under 35 U.S.C. 102(b)**

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Tani et al., (Anticancer Research, vol 13, page 1773-6, 1993) or Li et al., (Zhongguo Zhong Xi Yi Jie He Za Zhi, vol 16(4): 224-6, 1996, article in Chinese) as evidenced by Mesh word search (URL>[http://www.ncbi.nih.gov/entrez/query---](http://www.ncbi.nih.gov/entrez/query---mesh)mesh).

Tani et al., disclose a method for enhancing LAK activity by Lentinan, which is a polysaccharide containing extract of *Lentinus edodes* from cultured *Lentinus edodes* mycelium as evidenced by Mesh word search. The method disclosed by Tani et al., comprises isolating peripheral blood mononuclear cells (PBMC) from a subject and treating the cells with recombinant IL-2 and Lentinan, measuring, and comparing the cytotoxic activity of LAK to tumor cells enhanced by lentinan (page 1775, table 1 and figure 2).

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Li et al., et al., disclose a method for enhancing LAK activity by Lentinan, a polysaccharide containing extract from *Lentinus edodes* mycelium as evidence by Mesh word search (Exhibit A). The method disclosed by Li et al., comprises isolating Peripheral blood mononuclear cells from a subject and treating the cells with recombinant IL-2 and Lentinan. Li et al., also disclose that LAK activity is determined by cell-mediated lysis of tumor cells in release assay including using NK sensitive and NK resistant target cells (abstract).

2. ***Rejection under 35 U.S.C. 103***

Claim 1-2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamamoto et al., (Biosci Biotechno Biochem, vol 61, p1909-1912, 1997) in view of Liu et al., (Immunopharmacology, vol 40, page 187-198, 1998).

Yamamoto et al., teach cytotoxicity of lymphocytes, specifically NK cells, induced by an extract of culture medium of *Lentinus edodes* mycelia. Yamamoto et al., first teach how to prepare fractions from the extract of *Lentinus edodes* mycelia (page 1909, col 2, paragraph 1). Yamamoto et al., then teach a cytotoxicity assay against fibrosarcoma cells using lymphocytes, specifically NK cells, treated with a fraction of the extract of *Lentinus edodes* mycelia, JLS-18. Yamamoto et al., further teach that the extract of *Lentinus edodes* mycelia, specifically a fraction JLS-18, is effective activator of lymphocytes for their cytotoxicity against tumor cells (page 1911, col 1, paragraph 2 and figure 1).

Yamamoto et al., do not teach that extract of *Lentinus edodes* mycelia enhances cytotoxic activity of NK cells stimulated by IL-2 (LAK).

Liu et al., teach that IL-2 is augmented in human peripheral blood mononuclear cells (PBMC) treated with an extract of *Lentinus edodes* mycelia. Liu et al., teach that production of IL-2 in PBMC treated with crude extract of *Lentinus edodes* mycelia was measured by the levels of mRNA and protein in vitro and in vivo (page 196, section 3.1 and 3.2).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the method of Liu et al., (second reference) on IL-2 production by PBMC

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comprising NK cells treated by an extract of culture medium of *Lentinus edodes* mycelia to the method of Yamamoto et al., (primary reference) on determining the cytotoxicity of NK cells stimulated by IL-2 (LAK) enhanced by an extract of culture medium of *Lentinus edodes* mycelia. One of ordinary skill in the art would have been motivated with a reasonable expectation of success to combine the teachings of Yamamoto et al., to the teaching of Liu et al., to use the method to determine whether an extract of *Lentinus edodes* mycelia having LAK-enhancing effect because Yamamoto et al., have shown that cytotoxicity of lymphocytes, specifically NK cells, is induced by an extract of culture medium of *Lentinus edodes* mycelia and Liu et al., have shown that IL-2 is produced in human PBMC treated with an extract of *Lentinus edodes* mycelia, which suggests that the LAK cells exist or are produced in the PBMC treated with the extract.

### **Conclusion**

NO claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-4.30pm Monday to Friday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao, Ph.D.  
Examiner  
Art Unit 1642

LY

  
SHEELA HUFF  
PRIMARY EXAMINER